```
? ds

Set      Items   Description
S1     1442519   IMAG?
S2     2427556   TUMOR OR CANCER
S3      120726   S1 AND S2
S4     1041588   MIN OR MINUTES
S5        5072   S3 AND S4
S6      922002   IV OR INTRAVENOUS?
S7        1108   S5 AND S6
? s antibod?
      S8 1513563  ANTIBOD?
? s s7 and s8
            1108  S7
         1513563  S8
      S9     116  S7 AND S8
? s s9 and py<1998
Processing
             116  S9
        33352410  PY<1998
     S10      59  S9 AND PY<1998
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained i
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Fractional retention of technetium-99m-sestamibi as an index of P-glycoprotein expression in untreated breast **cancer** patients.

Del Vecchio S; Ciarmiello A; Pace L; Potena M I; Carriero M V; Mainolfi C ; Thomas R; D'Aiuto G; Tsuruo T; Salvatore M

Cattedra di Medicina Nucleare, Universita Federico II, Centro per lo Studio della Medicina Nucleare CNR, Naples, Italy.

Journal of nuclear medicine - official publication, Society of Nuclear Medicine (UNITED STATES) Sep **1997**, 38 (9) p1348-51, ISSN 0161-5505 Journal Code: 0217410

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The multidrug-resistant phenotype is characterized by the reduced intracellular retention of several structurally and functionally unrelated cytotoxic compounds due to the energy-dependent pump activity of P-glycoprotein (Pgp). Because 99mTc-sestamibi is a suitable transport substrate of Pgp, we tested whether the time-dependent fractional retention of this tracer could be used as an index of Pgp expression in untreated breast carcinomas. METHODS: Twenty-seven patients with histologically confirmed breast carcinoma were **intravenously** injected with 740 MBq (20 mCi) of 99mTc-sestamibi, and static planar **images** of the breast were obtained at 10, 60 and 240 **min**. The fractional retention of 99mTc-sestamibi was then calculated as the ratios between 60 and 10 **min** (R60/10) and between 240 and 10 **min** (R240/10) of decay-corrected counts/pixel registered in the region of interest drawn around the **tumor**. Surgically excised tumors were then obtained from each patient, and Pgp levels were determined using 125I-labeled MRK16 monoclonal **antibody** and in vitro quantitative autoradiography. RESULTS: The fractional retention of 99mTc-sestamibi at 60 and 240 **min** was significantly higher in tumors with low Pgp levels (Group I, n = 18) as compared to that measured in tumors with high Pgp expression (Group II, n = 9) ($p < 0.001$). In particular, R60/10 values were 0.86 and 0.59 in breast carcinomas of Groups I and II, respectively, whereas the values of R240/10 were 0.56 and 0.25 in low- and high-Pgp-expressing tumors, respectively. CONCLUSION: The determination of fractional retention of 99mTc-sestamibi may be used as a simple functional test for Pgp expression in untreated breast **cancer**. A preliminary estimate of the sensitivity and the specificity of the test indicates its potential use in clinical practice to identify patients with a high probability of developing multidrug resistance.

... retention of technetium-99m-sestamibi as an index of P-glycoprotein expression in untreated breast **cancer** patients.

Sep **1997**,

... expression in untreated breast carcinomas. METHODS: Twenty-seven patients with histologically confirmed breast carcinoma were **intravenously** injected with 740 MBq (20 mCi) of 99mTc-sestamibi, and static planar **images** of the breast were obtained at 10, 60 and 240 **min** . The fractional retention of 99mTc-sestamibi was then calculated as the ratios between 60 and 10 **min** (R60/10) and between 240 and 10 **min** (R240/10) of decay-corrected counts/pixel registered in the region of interest drawn around the **tumor**. Surgically excised tumors were then obtained from each patient, and Pgp levels were determined using 125I-labeled MRK16 monoclonal **antibody** and in vitro quantitative autoradiography. RESULTS: The fractional retention of 99mTc-sestamibi at 60 and 240 **min** was significantly higher in tumors with low Pgp levels (Group I, n = 18) as compared...

... sestamibi may be used as a simple functional test for Pgp expression in untreated breast **cancer** . A preliminary estimate of the sensitivity and the specificity of the test indicates its potential...

...29. The method of claim 1, wherein said region is in a **tumor** in said subject or a portion thereof...The method of claim 37, wherein the measuring of gamma ray emission to construct the **image** is done between about 5 **minutes** and about 2 hours after administration of the labeled annexin...

...The method of claim 39, wherein the measuring of gamma ray emission to construct the **image** is done about 1 hour after administration of the labeled annexin...

...41. The method of claim 37, where said radiation detector device is a 3-dimensional **imaging** camera...49. The method of claim 32, wherein the labeled annexin is administered **intravenously**.
60. The method of claim 32, wherein said region is in a **tumor** in said subject or a portion thereof...

...63. A method of **imaging** cell death in a **tumor** in a mammalian subject in vivo, comprising (a) administering to the subject, annexin labeled with...

Dialog Acc No: 3472099 IFI Acc No: 0108264
Document Type: C
METHOD OF **IMAGING** CELL DEATH IN VIVO; **IMAGING** APOPTOSIS BY ADMINISTERING TO THE PATIENT, ANNEXIN LABELED WITH A RADIONUCLIDE, MEASURING RADIATION EMISSION FROM RADIONUCLIDE WITH RADIO DETECTOR TO CONSTUCT AN **IMAGE** OF RADIATION EMISSION WHICH REPRESENT CELL DEATH OF THE MAMMAL
Inventors: Blankenberg Francis G (US); Katsikis Peter D (US); Strauss H William (US); Tait Jonathan F (US)
Assignee: Stanford, Leland Jr University Trustees; Washington, University of
Assignee Code: 02937 49136
Publication (No,Date), Applic (No,Date):
US 6197278 20010306 US 9869878 19980429
Publication Kind: B
Calculated Expiration: 20180429
(Cited in 001 later patents)
Priority Applic(No,Date): US 9869878 19980429
Provisional Applic(No,Date): US 60-45399 19970430

Abstract: A method of **imaging** apoptosis in vivo, using radiolabeled annexin, is described.

METHOD OF **IMAGING** CELL DEATH IN VIVO...

...**IMAGING** APOPTOSIS BY ADMINISTERING TO THE PATIENT, ANNEXIN LABELED WITH A RADIONUCLIDE, MEASURING RADIATION EMISSION FROM RADIONUCLIDE WITH RADIO DETECTOR TO CONSTUCT AN **IMAGE** OF RADIATION EMISSION WHICH REPRESENT CELL DEATH OF THE MAMMAL

Abstract: A method of **imaging** apoptosis in vivo, using radiolabeled annexin, is described.

Exemplary Claim: D R A W I N G

1. A method of **imaging** cell death in a nucleated cell within a region of a mammalian subject in vivo...

...emission from the radionuclide in the subject, with the radiation detector device, to construct an **image** of radiation emission, wherein said **image** is a representation of cell death in said nucleated cell of said mammalian subject.
32. A method of **imaging** cell death in a nucleated cell within a region of a mammalian subject in vivo...

...biocompatible radionuclide, (b) measuring radiation emission from the radionuclide in the subject, to construct an **image** of radiation emission, wherein said **image** is a representation of cell death in said nucleated cell of said mammalian subject.
Non-exemplary Claims: ...The method of claim 6, wherein the measuring of gamma ray emission to construct the **image** is done between about 5 **minutes** and about 2 hours after administration of the labelled annexin...

...The method of claim 8, wherein the measuring of gamma ray emission to construct the **image** is done about 1 hour after administration of the labelled annexin...

...13. The method of claim 1, where said radiation detector device is a 3-dimensional **imaging** camera...17. The method of claim 1, wherein the labeled annexin is administered **intravenously**.
...

Chengazi V U; Feneley M R; Ellison D; Stalteri M; Granowski A; Granowska M; Nimmon C C; Mather S J; Kirby R S; Britton K E

Department of Nuclear Medicine, St. Bartholomew's Hospital, London, United Kingdom.

Journal of nuclear medicine - official publication, Society of Nuclear Medicine (UNITED STATES) May **1997**, 38 (5) p675-82, ISSN 0161-5505 Journal Code: 0217410

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

To evaluate the performance of the 99mTc-labeled monoclonal **antibody** CYT-351 in visualizing prostate **cancer** , radioimmunoscintigraphy (RIS) was performed in 35 patients. METHODS: **Antibody** (0.5 mg) labeled with 600 MBq 99mTc was injected **intravenously** after obtaining informed consent. Planar and SPECT **imaging** was performed at 10 **min** and 6-8 and 22-24 hr postinjection. The scans were evaluated for visualization of the primary focus or local recurrence, extraprostatic invasion, lymph node involvement and uptake in bone and soft tissue metastases. RESULTS: Thirty-six studies in 35 patients were performed. In 13/14 evaluable studies with clinically localized prostate **cancer** , RIS had a true-positive rate of 92% (12/13). In eight patients with previous incidental carcinoma detected during transurethral resection undertaken for clinically benign disease, there were 86% true-positive results (6/7) and one true-negative result, which were confirmed by systematic needle biopsies. In six patients with evidence of local recurrence after a previous radical prostatectomy, the true-positive rate was 100% (6/6), which was confirmed by raised or rising prostate-specific antigen levels (PSA) and/or by biopsy. In the eight patients with known metastases, the disease was visualized in 4/4 with progression but not in the 3/3 with regression; one patient demonstrated regressing disease as determined by PSA levels. The overall accuracy was 92%. CONCLUSION: RIS with 99mTc CYT-351 is capable of

7/3,K,AB/26 (Item 3 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 1528011 IFI Acc No: 8410307
Document Type: C
USE OF METAL CHELATE CONJUGATED MONOCLONAL **ANTIBODIES**; DIAGNOSIS, TREATMENT OF **CANCER**
Inventors: GANSOW OTTO A (US); STRAND METTE (US)
Assignee: UNASSIGNED OR ASSIGNED TO INDIVIDUAL
Assignee Code: 68000 Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 4454106 **19840612** US 82386109 19820607
Publication Kind: A
Calculated Expiration: 20020607
(Cited in 074 later patents) Document Type: CERTIFICATE OF CORRECTION
Certificate of Correction Date: 19841120
Priority Applic(No,Date): US 82386109 19820607

Abstract: Therapeutic and diagnostic methods employing metal chelate conjugated monoclonal **antibodies** are described. Metals employed in therapeutic conjugated **antibodies** include alpha particle, beta particle or Auger electron emitting isotopes. Diagnostic methods may be either in vivo or in vitro. Chelated metals employed in diagnostic techniques may include, inter alia, gamma or positron emitting metals as well as fluorogenic or paramagnetic metals.

USE OF METAL CHELATE CONJUGATED MONOCLONAL **ANTIBODIES**; ...

7/3,K,AB/25 (Item 2 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 1838877 IFI Acc No: 8804854
Document Type: C
TRACE-LABELED CONJUGATES OF METALLOTHIONEIN AND TARGET-SEEKING BIOLOGICALLY ACTIVE MOLECULES; MEDICAL DIAGNOSIS
Inventors: TOLMAN GLEN L (US)
Assignee: DU PONT DE NEMOURS, E I & CO
Assignee Code: 25048 Document Type: REASSIGNED
Publication (No,Date), Applic (No,Date):
US 4732864 **19880322** US 83539733 19831006
Publication Kind: A
Calculated Expiration: 20050322
(Cited in 048 later patents)
Priority Applic(No,Date): US 83539733 19831006

Abstract: Conjugates of target-seeking biologically active molecules and metallothionein in which all or part of the metal in the metallothionein is suitable for diagnostic or therapeutic applications.

Publication (No,Date), Applic (No,Date):
...**19880322**

Exemplary Claim: ...CONJUGATE OF (A) A TARGET-SEEKING BIOLOGICALLY ACTIVE MOLECULE SELECTED FROM THE GROUP CONSISTING OF **ANTIBODIES**, **ANTIBODY** FRAGMENTS, HORMONES, PEPTIDES, PROTEINS AND DRUGS WHICH BIND TO RECEPTORS AND LOCALIZE IN CERTAIN ORGANS...
Non-exemplary Claims: ...203, Ru-97, Hg-197, Ag-111, Au-198, Pd-103, Cu-67, Re-188, **Bi-212**, Os-191...

7/3,K,AB/24 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2004 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 2940249 IFI Acc No: 9804038
Document Type: C
BIOTIN COMPOUNDS FOR TARGETTING TUMORS AND SITES OF INFECTION; CONJUGATING A THERAPEUTIC AGENT TO BIOTIN TO FORM A COMPOUND THAT HAS A SPECIFICITY FOR THE SITE OF INFECTION
Inventors: Babich John W (US); Elmaleh David R (US); Fischman Alan J (US); Shoup Timothy M (US)
Assignee: JMDE Trust The
Assignee Code: 44549
Publication (No,Date), Applic (No,Date):
US 5716594 **19980210** US 96725060 19961002
Publication Kind: A
Calculated Expiration: 20140606
(Cited in 003 later patents)
Continuation Pub(No),Applic(No,Date): ABANDONED US 95461622 19950605
Cont.-in-part Pub(No),Applic(No,Date): ABANDONED US 94254260 19940606; ABANDONED US 94265516 19940624
Priority Applic(No,Date): US 96725060 19961002; US 95461622 19950605; US 94254260 19940606; US 94265516 19940624
Abstract: Novel biotin amide analogs that are useful for targeting therapeutic and imaging agents to sites of infection and tumors in vivo are disclosed.

7/3,K,AB/19 (Item 16 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2004 Inst for Sci Info. All rts. reserv.

01006255 Genuine Article#: FN661 Number of References: 45
Title: NEWER APPROACHES TO THE RADIOLABELING OF MONOCLONAL-**ANTIBODIES** BY USE OF METAL-CHELATES (Abstract Available)
Author(s): GANSOW OA
Corporate Source: NIH,RADIAT ONCOL BRANCH,CHEM SECT,BLDG 10,RM B3B69,9000 ROCKVILLE PIKE/BETHESDA//MD/20892
Journal: NUCLEAR MEDICINE AND BIOLOGY-INTERNATIONAL JOURNAL OF RADIATION APPLICATIONS ANDINSTRUMENTATION PART B, **1991**, V18, N4, P369-381
Language: ENGLISH Document Type: ARTICLE
Abstract: Monoclonal **antibodies** (mAbs) radiolabeled by use of metal chelators are being investigated in the laboratory for use in clinical trials. In-111 is presently employed for diagnostic scintigraphy, but its applications are limited by substantive and persistant uptake of radiometal in the liver. Much current research is focused on performing **cancer** therapy with Y-90 and **Bi-212** chelate-linked mAbs. This report chronicles the development and evaluation of chelating agents for In-111-radioimmunoimaging and Y-90- and **Bi-212**-radioimmunotherapy.

Title: NEWER APPROACHES TO THE RADIOLABELING OF MONOCLONAL-**ANTIBODIES** BY USE OF METAL-CHELATES
, **1991**

7/3,K,AB/18 (Item 15 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2004 Inst for Sci Info. All rts. reserv.

01210389 Genuine Article#: GE516 Number of References: 16
Title: AN EFFECTIVE CHELATING AGENT FOR LABELING OF MONOCLONAL-**ANTIBODY** WITH **BI-212** FOR ALPHA-PARTICLE MEDIATED RADIOIMMUNOTHERAPY (Abstract Available)
Author(s): BRECHBIEL MW; PIPPIN CG; MCMURRY TJ; MILENIC D; ROSELLI M; COLCHER D; GANSOW OA
Corporate Source: NCI,RADIAT ONCOL BRANCH,INORGAN & RADIOIMMUNE CHEM SECT/BETHESDA//MD/20892; NCI,RADIAT ONCOL BRANCH,INORGAN & RADIOIMMUNE CHEM SECT/BETHESDA//MD/20892; NCI,TUMOR IMMUNOL & BIOL LAB/BETHESDA//MD/20892
Journal: JOURNAL OF THE CHEMICAL SOCIETY-CHEMICAL COMMUNICATIONS, **1991**, N17, P1169-1170
Language: ENGLISH Document Type: ARTICLE
Abstract: The ligand N[2-amino-3-(p-isothiocyanatophenyl)propyl]-(+/-)-trans-1,2-diaminocyclohexane-N,N',N''-pentaacetic acid has been synthesized and linked to IgG and to monoclonal **antibody** B72.3, and labelled with Bi-206 and **Bi-212** to demonstrate the in vivo stability of the label and its utility for **Bi-212**-radioimmunotherapy.

Title: AN EFFECTIVE CHELATING AGENT FOR LABELING OF MONOCLONAL-**ANTIBODY** WITH **BI-212** FOR ALPHA-PARTICLE MEDIATED RADIOIMMUNOTHERAPY
, **1991**
...Abstract: N,N',N''-pentaacetic acid has been synthesized and linked to IgG and to monoclonal **antibody** B72.3, and labelled with Bi-206

7/3,K,AB/14 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2004 Inst for Sci Info. All rts. reserv.

02423338 Genuine Article#: KZ773 Number of References: 127
Title: EXPERIMENTAL RADIOIMMUNOTHERAPY (Abstract Available)
Author(s): BUCHSBAUM DJ; LANGMUIR VK; WESSELS BW
Corporate Source: UNIV ALABAMA,DEPT RADIAT ONCOL,619 S 19TH ST/BIRMINGHAM//AL/35233; SRI INT,DIV LIFE SCI/MENLO PK//CA/94025; GEORGE WASHINGTON UNIV,MED CTR,DEPT RADIOL/WASHINGTON//DC/20037
Journal: MEDICAL PHYSICS, **1993**, V20, N2 (MAR-APR), P551-567
ISSN: 0094-2405
Language: ENGLISH Document Type: REVIEW
Abstract: Radiolabeled monoclonal **antibodies** have been used for radioimmunotherapy studies with human **tumor** spheroids and murine and human **tumor** xenografts in experimental animals. This paper reviews the work that has been performed in these models with different types of **cancer**, and highlights those papers that have presented dosimetry estimates and attempts to correlate the findings. Radioimmunotherapy studies in multicell spheroids, as a model for micrometastases, have been performed in human neuroblastoma, colon **cancer**, and melanoma cell lines using I-131, I-25, Re-186, and **Bi-212**-labeled **antibodies**. The uniform geometry of the spheroid has allowed radiation dose estimates to be made. Up to three logs of cell kill have been achieved with I-131 and Re-186-specific **antibody** with minimal toxicity from labeled nonspecific **antibody**, but **Bi-212-antibody** had little effect because of its short half-life as shown by Langmuir. It appears that the two most important factors for therapeutic efficacy in this model are good penetration of the radiolabeled **antibody** and an adequate radionuclide half-life to allow penetration of the immunoconjugate prior to significant radionuclide decay. Radioimmunotherapy studies in animals bearing transplants of colon **cancer**, leukemia, lymphoma, hepatoma, renal cell **carcinoma**, neuroblastoma, glioma, mammary **carcinoma**, small cell lung **carcinoma**, cervical **carcinoma**, ovarian **carcinoma**, and bladder **cancer** have been performed with I-131, Y-90, Re-186, Sm-153, and Lu-177 beta emitting, and **Bi-212** alpha emitting radionuclides conjugated to monoclonal **antibodies**. A few studies compared different radionuclides in the same model system. The approaches that have been used in these studies to estimate **tumor** dosimetry include the MIRD approach, thermoluminescent dosimetry, autoradiography, and comparison to external irradiation. The majority of investigators have estimated the dose to **tumor** and normal organs using MIRD-based calculations (time-activity curve and equilibrium dose constant method). The range of **tumor** doses has been between 17 and 11 171 mGy/MBq of administered radioactivity. The effectiveness of radiolabeled monoclonal **antibody** therapy depends on a number of factors relating to the **antibody** such as specificity, affinity, and immunoreactivity. The density, location, and heterogeneity of expression of **tumor**-associated antigen within tumors will affect the localization and therapeutic efficacy of radiolabeled **antibodies**, as will physiological factors such as the **tumor** vascularity, blood flow, and permeability. These factors are discussed and examples are presented. In the future, it is recommended that investigators make comparisons of different radionuclides in the same system, which should include an analysis of the relative toxicity. It is also recommended that comparisons to external beam radiation be made for both **tumor** and normal tissue damage. It is also recommended that investigators look at radiation dose heterogeneity using thermoluminescent dosimeters and autoradiography, so that the range of **tumor** radiation dose and dose-rate is reported. It is hoped that an answer to how heterogeneity

in radiolabeled **antibody** deposition in experimental tumors and spheroids affects absorbed dose distribution and the radiobiological consequences will be understood.

It is also hoped that a definitive answer will be obtained for what radionuclides and forms of **antibody** are optimum for radioimmunotherapy of leukemias, micrometastases, and solid tumors, and most importantly how best to apply these techniques and information to the treatment of **cancer** clinically.

, **1993**

Abstract: Radiolabeled monoclonal **antibodies** have been used for radioimmunotherapy studies with human **tumor** spheroids and murine and human **tumor** xenografts in experimental animals. This paper reviews the work that has been performed in these models with different types of **cancer**, and highlights those papers that have presented dosimetry estimates and attempts to correlate the findings...

...in multicell spheroids, as a model for micrometastases, have been performed in human neuroblastoma, colon **cancer**, and melanoma cell lines using I-131, I-25, Re-186, and **Bi-212**-labeled **antibodies**. The uniform geometry of the spheroid has allowed radiation dose estimates to be made. Up...

...three logs of cell kill have been achieved with I-131 and Re-186-specific **antibody** with minimal toxicity from labeled nonspecific **antibody**, but **Bi-212-antibody** had little effect because of its short half-life as shown by Langmuir. It appears...

...most important factors for therapeutic efficacy in this model are good penetration of the radiolabeled **antibody** and an adequate radionuclide half-life to allow penetration of the immunoconjugate prior to significant radionuclide decay. Radioimmunotherapy studies in animals bearing transplants of colon **cancer**, leukemia, lymphoma, hepatoma, renal cell **carcinoma**, neuroblastoma, glioma, mammary **carcinoma**, small cell lung **carcinoma**, cervical **carcinoma**, ovarian **carcinoma**, and bladder **cancer** have been performed with I-131, Y-90, Re-186, Sm-153, and Lu-177 beta emitting, and **Bi-212** alpha emitting radionuclides conjugated to monoclonal **antibodies**. A few studies compared different radionuclides in the same model system. The approaches that have been used in these studies to estimate **tumor** dosimetry include the MIRD approach, thermoluminescent dosimetry, autoradiography, and comparison to external irradiation. The majority of investigators have estimated the dose to **tumor** and normal organs using MIRD-based calculations (time-activity curve and equilibrium dose constant method). The range of **tumor** doses has been between 17 and 11 171 mGy/MBq of administered radioactivity. The effectiveness of radiolabeled monoclonal **antibody** therapy depends on a number of factors relating to the **antibody** such as specificity, affinity, and immunoreactivity. The density, location, and heterogeneity of expression of **tumor**-associated antigen within tumors will affect the localization and therapeutic efficacy of radiolabeled **antibodies**, as will physiological factors such as the **tumor** vascularity, blood flow, and permeability. These factors are discussed and examples are presented. In the...

...toxicity. It is also recommended that comparisons to external beam radiation be made for both **tumor** and normal tissue damage. It is also recommended that investigators look at radiation dose

03343143 Genuine Article#: NY302 Number of References: 27
Title: PB-**212**/**BI**-**212**-EDTMP-SYNTHESIS AND BIODISTRIBUTION OF A NOVEL BONE SEEKING ALPHA-EMITTING RADIOPHARMACEUTICAL (Abstract Available)
Author(s): HASSFJELL SP; HOFF P; BRULAND OS; ALSTAD J
Corporate Source: UNIV OSLO,DEPT NUCL CHEM,POB 1033 BLINDERN/N-0315 OSLO//NORWAY/; NORWEGIAN RADIUM HOSP,DEPT ONCOL/N-0310 OSLO//NORWAY/
Journal: JOURNAL OF LABELLED COMPOUNDS & RADIOPHARMACEUTICALS, **1994**, V34, N8 (AUG), P717-734
ISSN: 0362-4803
Language: ENGLISH Document Type: ARTICLE
Abstract: At present, haematological toxicity is dose limiting in radionuclide therapy of bone metastases, and there is a need for radiopharmaceuticals with improved tumour/bone marrow dose ratios. Therefore, a-emitters e.g. **Bi**-**212** may be more suitable than beta-emitters, because of the short range and high LET values of alpha-particles. In this study, **Bi**-**212** and its mother nuclide Pb-212 were produced in an isotope generator by collecting gaseous Rn-220 emanating from barium (Th-228) stearate. The carrier-free Pb-**212**/**Bi**-**212** were bound to the chelating bone-seeking compound ethylene-diamine-tetra(methylene-phosphonic acid) (EDTMP) with 90% yield. The biodistribution in Balb/c mice was investigated by injecting 100 mul of a saline PBS buffer 0.020 M in EDTMP and 10 MBq/ml in Pb-**212**/**Bi**-**212**. Mice were killed in groups of three at 0.5, 2, 13 and 24 h post-injection times. Both Pb-**212** EDTMP and **Bi**-**212**-EDTMP localised strongly in the skeleton, especially in the femur, at all time points measured, with the % of injected dose per gram (%ID/g) as high as 15 for Pb-212 and 13 for **Bi**-**212**

394337 Genuine Article#: YP202 Number of References: 37
Title: Radioimmunotherapy targeting of HER2/neu oncoprotein on ovarian **tumor** using lead-212-DOTA-AE1 (ABSTRACT AVAILABLE)
Author(s): Horak E; Hartmann F; Garmestani K; Wu CC; Brechbiel M; Gansow OA ; Landolfi NF; Waldmann TA (REPRINT)
Corporate Source: NCI,METAB BRANCH, NIH, BLDG 10, ROOM 4N115/BETHESDA//MD/20892 (REPRINT); NCI,METAB BRANCH, NIH/BETHESDA//MD/20892; NCI,INORGAN & RADIOIMMUNE CHEM SECT, RADIAT ONCOL BRANCH, NIH/BETHESDA//MD/20892; PROT DESIGN LABS INC,/MT VIEW//CA/
Journal: JOURNAL OF NUCLEAR MEDICINE, **1997**, V38, N12 (DEC), P 1944-1950
ISSN: 0161-5505 Publication date: 19971200
Publisher: SOC NUCLEAR MEDICINE INC, 1850 SAMUEL MORSE DR, RESTON, VA 20190-5316
Language: English Document Type: ARTICLE
Abstract: The specificity, toxicity and efficacy of lead (Pb-212) radioimmunotherapy were evaluated in nude mice bearing the SK-OV-3 human ovarian **tumor** cell line expressing the HER2/neu proto-oncogene. Methods: The therapeutic agent used was the **tumor** -specific anti-HER2/neu monoclonal **antibody** AE1 conjugated to Pb-**212**, **Bi-212** being the daughter and thus the source of the alpha-particle and beta emissions. A bifunctional derivative of tetraazacyclododecanetetraacetic acid (p-SCN-Bz-DOTA) was used to couple Pb-212 to the anti-HER2/neu monoclonal **antibody** AE1. The chelating agent did not alter the binding affinity to its antigenic target or the pharmacokinetics and tissue distribution of the AE1 **antibody**, Toxicity and therapeutic efficacy of Pb-212-AE1 were evaluated in nude mouse ascites or solid **tumor** models, wherein SK-OV-3 cells were administered i.p. or s.c., respectively. Results: The dose-limiting acute toxicity after i.v. administration of Pb-212-AE1 was bone marrow suppression, which was observed at doses above 25 mu Ci. Therefore, doses of 10 and 20 mu Ci were used in efficacy trials. The i.p. administration of Pb-212-AE1 3 days after i.p. **tumor** inoculation led to a significant (p(2) = 0.015) prolongation of **tumor**-free survival. In a second model, i.v. treatment with Pb-212-AE1 3 days after s.c. **tumor** inoculation prevented subsequent **tumor** development in all animals treated with 10 or 20 mu Ci of Pb-212-AE1 (p(2) = 0.002 compared to control groups). This efficacy in the adjuvant setting was **antibody** specific because treatments with equivalently labeled control **antibody** or unlabeled AE1 **antibody** or no treatment were less effective. The rate of growth of small (mean **tumor** volume, 15 mm(3)) SK-OV-3 tumors was modestly inhibited. However, **tumor** growth was not inhibited in mice bearing larger (mean **tumor** volume, 146 mm(3)) SK-OV-3 tumors by the administration of a single dose of 10 or 20 mu Ci of Pb-212-AE1. Conclusion: Lead-212-AE1 as an intact radiolabeled monoclonal **antibody** may be of only modest value in the therapy of bulky solid tumors due to the short physical half-life of Pb-212 and time required to achieve a useful **tumor** -to-normal tissue ratio of radionuclide after administration. However, the radiolabeled monoclonal **antibody** may be useful in therapy of tumors in the adjuvant setting. Furthermore, Pb-212 may be of value in select situations, including treatment of leukemia, intercavitary therapy or strategies that target vascular endothelial cells of tumors.

Title: Radioimmunotherapy targeting of HER2/neu oncoprotein on ovarian **tumor** using lead-212-DOTA-AE1
, **1997**
...Abstract: Pb-212) radioimmunotherapy were evaluated in nude mice bearing the SK-OV-3 human ovarian **tumor** cell line expressing the HER2/neu proto-oncogene. Methods: The therapeutic agent used was the **tumor** -specific anti-HER2/neu monoclonal **antibody** AE1 conjugated to Pb-**212**, **Bi-212** being the daughter and thus the source of

the alpha-particle and beta emissions. A...
...SCN-Bz-DOTA) was used to couple Pb-212 to the anti-HER2/neu monoclonal **antibody** AE1. The chelating agent did not alter the binding affinity to its antigenic target or the pharmacokinetics and tissue distribution of the AE1 **antibody**, Toxicity and therapeutic efficacy of Pb-212-AE1 were evaluated in nude mouse ascites or solid **tumor** models, wherein SK-OV-3 cells were administered i.p. or s.c., respectively. Results...

...efficacy trials. The i.p. administration of Pb-212-AE1 3 days after i.p. **tumor** inoculation led to a significant (p(2) = 0.015) prolongation of **tumor**-free survival. In a second model, i.v. treatment with Pb-212-AE1 3 days after s.c. **tumor** inoculation prevented subsequent **tumor** development in all animals treated with 10 or 20 mu Ci of Pb-212-AE1 (p(2) = 0.002 compared to control groups). This efficacy in the adjuvant setting was **antibody** specific because treatments with equivalently labeled control **antibody** or unlabeled AE1 **antibody** or no treatment were less effective. The rate of growth of small (mean **tumor** volume, 15 mm(3)) SK-OV-3 tumors was modestly inhibited. However, **tumor** growth was not inhibited in mice bearing larger (mean **tumor** volume, 146 mm(3)) SK-OV-3 tumors by the administration of a single dose...
...mu Ci of Pb-212-AE1. Conclusion: Lead-212-AE1 as an intact radiolabeled

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? s bi(2n)(212 or 213)
          652112  BI
           25055  212
           20249  213
      S1     425  BI(2N)(212 OR 213)
? s antibod?
      S2 1513739  ANTIBOD?
? s s1 and s2
             425  S1
         1513739  S2
      S3     207  S1 AND S2
? s cancer or tumor or carcinoma or malignan?
         1389241  CANCER
         1477484  TUMOR
          831216  CARCINOMA
          551991  MALIGNAN?
      S4 3008649  CANCER OR TUMOR OR CARCINOMA OR MALIGNAN?
? s s3 and s4
             207  S3
         3008649  S4
      S5     140  S3 AND S4
? s s5 and py<=1998
Processing
             140  S5
        35476986  PY<=1998
      S6      29  S5 AND PY<=1998
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S7      26  RD (unique items)
? t s7/3,k,ab/1-26

 7/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

13022893   PMID: 8679266
  Radioimmunotherapy of solid cancers: A review.
  Kairemo K J
  Department of Oncology, Helsinki University Central Hospital, Helsinki,
Finland.
  Acta oncologica (Stockholm, Sweden) (NORWAY) 1996, 35 (3)
 p343-55, ISSN 0284-186X Journal Code: 8709065
  Document type: Journal Article; Review; Review, Tutorial
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Depending on radionuclide characteristics, radioimmunotherapy (RIT)
relies on radioactivity to destroy cells distant from immunotargeted cells.
Therefore, even heterogeneous tumors (for antigen recognition) can be
treated, because not all cells have to be targeted. Substantial complete
response rates have been reported in patients with non-Hodgkin's lymphoma.
Much more modest results have been reported for patients with bulky solid
tumors, e.g. adenocarcinomas. The radiation doses delivered by targeting
antibodies are generally too low to achieve major therapeutic
responses. Dose escalation is limited by myelotoxicity, and higher doses
need to be delivered to neoplasms less radiosensitive than lymphomas.
Various trials for both systemic and regional RIT have been reported on.
Intraperitoneal administration has been applied for colorectal and ovarian
carcinomas. Our own results indicate that, e.g., intraperitoneal
pseudomyxoma can be treated with RIT. Myelotoxicity can be reduced by anti-
```

antibody-enhancement, 2- and 3-step strategies, bispecific monoclonal **antibodies** (MAbs), and extracorporeal immunoadsorption. The radionuclide has to be selected properly for each purpose; it can be a beta-emitter, e.g. I-131, Y-90, Re-188, Re-186, Lu-177 or Sm-153, an alpha-emitter At-211 or **Bi-212** or an Auger-emitter, e.g. I-125, I-123. One major problem with RIT, besides slow penetration rate into **tumor** tissue and low **tumor**-to-normal tissue ratio, is the HAMA response, which can be partly avoided by the use of humanized MAbs and immunosuppression. However, RIT will be, because of all the recent developments, an important form of **cancer** management.

1996,
... for patients with bulky solid tumors, e.g. adenocarcinomas. The radiation doses delivered by targeting **antibodies** are generally too low to achieve major therapeutic responses. Dose escalation is limited by myelotoxicity...

... e.g., intraperitoneal pseudomyxoma can be treated with RIT. Myelotoxicity can be reduced by anti-**antibody**-enhancement, 2- and 3-step strategies, bispecific monoclonal **antibodies** (MAbs), and extracorporeal immunoadsorption. The radionuclide has to be selected properly for each purpose; it...

...Re-188, Re-186, Lu-177 or Sm-153, an alpha-emitter At-211 or **Bi-212** or an Auger-emitter, e.g. I-125, I-123. One major problem with RIT, besides slow penetration rate into **tumor** tissue and low **tumor** -to-normal tissue ratio, is the HAMA response, which can be partly avoided by the...

... immunosuppression. However, RIT will be, because of all the recent developments, an important form of **cancer** management.
; Adenocarcinoma--radiotherapy--RT; **Antibodies**, Anti-Idiotypic --biosynthesis--BI; Bone Marrow--radiation effects--RE; Colorectal Neoplasms--radiotherapy--RT; Injections, Intraperitoneal...
Chemical Name: **Antibodies**, Anti-Idiotypic; Radioisotopes

7/3,K,AB/2 (Item 1 from file: 55)
DIALOG(R)File 55:Biosis Previews(R)
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0011543383 BIOSIS NO.: 199800337630
Radiation dosimetry for a **Bi-213** monoclonal **antibody** bound to membranes of monolayer and spheroid cultures of **tumor** cells
AUTHOR: Stabin M (Reprint); Kennel S; Mirzadeh S
AUTHOR ADDRESS: Oak Ridge Inst. Science Education, Oak Ridge, TN, USA**USA
JOURNAL: Journal of Nuclear Medicine 39 (5 SUPPL.): p184P May, 1998
1998
MEDIUM: print
CONFERENCE/MEETING: 45th Annual Meeting of the Society of Nuclear Medicine Toronto, Ontario, Canada June 7-11, 1998; 19980607
SPONSOR: Society of Nuclear Medicine
ISSN: 0161-5505
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

Radiation dosimetry for a **Bi-213** monoclonal **antibody** bound to membranes of monolayer and spheroid cultures of **tumor**

ONTRAST MEDIUM FOR NEAR INFRARED DIAGNOSIS; POLYMETHINE WITH SUITABLE PHOTOPHYSICAL AND PHARMACOLOGICAL PROPERTIES, USED IN FLUORESCENCE AND TRANSILLUMINATION DIAGNOSTICS

Inventors: Heldmann Dieter (DE); Licha Kai (DE); Riefke Bjorn (DE); Sudmann Violetta (DE); Weitschiess Werner (DE)
Assignee: Institut fur Diagnostikforschung GmbH DE
Assignee Code: 33289

Publication (No,Date), Applic (No,Date):
US 6319488 20011120 US 9851511 19980409
Publication Kind: B
Calculated Expiration: 20160926
PCT Pub(No,Date),Applic(No,Date): WO 9713490 **19970417** WO 96DE1878 19960926
Section 371: 19980409
Section 102(e):19980409
Priority Applic(No,Date): DE 19539409 19951011

Abstract: This invention relates to colloidal systems charged with polymethine dyes and having suitable photophysical and pharmacological properties, their use as a contrast medium in fluorescence and transillumination diagnostics in the near infrared spectral range, as well as methods for their production.

...PCT Pub(No,Date),Applic(No,Date): **19970417**

Exemplary Claim: ...combination, wherein said target tissue is selected from the group consisting of inflamed tissue and **tumor** tissue, said in vivo contrast medium comprising a colloidal system with particles having a size...

Non-exemplary Claims: ...wavelength range, said target tissue is selected from the group consisting of inflamed tissue and **tumor** tissue, said method comprising the steps of: (a) preparing an in vivo contrast medium comprising...

...by liver tissue at a faster rate than degradation by said target tissue; (b) performing **intravenous** administration of said in vivo contrast medium into an organism; (c) sufficiently irradiating said organism...

...medium to fluoresce; and (d) scanning said irradiated organism using a CCD camera to obtain **images** of said in vivo contrast medium to detect the diseased tissue...

...7. The method of claim 6 further comprising repeating steps (c) and (d) about 10 **minutes** after step (a), 1 hour after step (a), 18 hours after step (a), and 24...

...combination, wherein said target tissue is selected from the group consisting of inflamed tissue and **tumor** tissue, said in vivo contrast medium comprising a colloidal system, said colloidal system having a...

...9. A method for **imaging tumor** tissue comprising the steps of: (a) performing **intravenous** administration of an in vivo contrast medium into a body suspected of harboring **tumor** tissue, said in vivo contrast medium comprising colloidal system with a particle size range from...

...nm to 1200 nm, said in vivo contrast medium being amenable to accumulation in said **tumor** tissue, said in vivo contrast medium being amenable to degradation by liver tissue at a faster rate than degradation by said **tumor** tissue; (b) irradiating said body with monochrome light in the wavelength range of about 600...

...step (b) to absorb and/or fluoresce; and (c) scanning said irradiated body to yield **images** of said **tumor** tissue in said body...

...method of claim 9, wherein step (c) further comprise

Rapid imaging of human melanoma xenografts using an scFv fragment of the human monoclonal **antibody** H11 labelled with 111In.

Reilly R M; Maiti P K; Kiarash R; Prashar A K; Fast D G; Entwistle J; Dan ; Narang S A; Foote S; Kaplan H A

Division of Nuclear Medicine, Toronto General Hospital, University Health Network, ON, Canada. raymond.reilly@utoronto.ca

Nuclear medicine communications (England) May 2001, 22 (5) p587-95, ISSN 0143-3636 Journal Code: 8201017

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

H11 is a human IgM monoclonal **antibody** which recognizes a novel tumour-associated antigen expressed on melanoma, glioma, breast **cancer**, colon **cancer**, prostate **cancer**, lung **cancer** and B-cell lymphoma. In this study, a recombinant single-chain Fv (scFv) fragment of H11 labelled with 111In was investigated for tumour imaging in athymic mice implanted subcutaneously with A-375 human melanoma xenografts. H11 scFv was derivatized with diethylenetriaminepentaacetic acid (DTPA) for labelling with 111In. The immunoreactivity of DTPA-H11 scFv against A-375 cells in vitro ranged from 23% to 36%. 111In-DTPA-H11 scFv was rapidly eliminated from the **blood** and most normal tissues (except the kidneys) **reaching** maximum tumour/**blood** ratios of 12:1 at 48 **h** post-injection. Tumours were imaged as early as 40 **min** after injection. The kidneys accumulated the highest concentration of radioactivity (up to 185% injected dose/g). Tumour uptake was 1-3% injected dose/g. The whole-body radiation absorbed dose predicted for administration of 185 MBq of 111In-DTPA-H11 scFv to humans was 37 mSv. The radiation absorbed dose estimates for the kidneys, spleen and intestines were 405 mSv, 698 mSv and 412 mSv, respectively. The results of this preclinical study and a concurrent phase I trial suggest a promising role for H11 scFv for tumour imaging.

Set	Items	Description
S1	1510505	ANTIBOD?
S2	80550	PHARMA?(5N)KINETIC??
S3	3412	S1 AND S2
S4	2924641	CANCER OR TUMOR OR TARGET
S5	718	S3 AND S4
S6	7370514	TIME OR H OR HOUR OR MIN OR MINUTE
S7	469	S5 AND S6
S8	616345	REACH?
S9	25	S7 AND S8
S10	25	RD (unique items)
S11	4381725	BLOOD OR CIRCULATION
S12	9	S10 AND S11
S13	9	RD (unique items)

Treatment-related parameters predicting efficacy of Lym-1 radioimmunotherapy in patients with B-lymphocytic malignancies.

Lamborn K R; DeNardo G L; DeNardo S J; Goldstein D S; Shen S; Larkin E C; Kroger L A

Brain Tumor Research Center, Department of Neurological Surgery, University of California San Francisco Medical Center, San Francisco, California 94143, USA.

Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Aug 1997, 3 (8) p1253-60, ISSN 1078-0432 Journal Code: 9502500

Contract/Grant No.: CA 47829; CA; NCI

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

This study was designed to evaluate dosimetric, pharmacokinetic, and other treatment-related parameters as predictors of outcome in patients with advanced B-lymphocytic malignancies. Fifty-seven patients were treated with radiolabeled Lym-1 **antibody** in early phase trials between 1985 and 1994. Logistic regression and proportional hazards models were used to evaluate treatment parameters for their ability to predict outcome, taking into account patient risk group based on Karnofsky performance status and serum lactic dehydrogenase. The occurrence of a partial or complete response (31 of 57 patients) and development of human antimouse **antibody** (HAMA) predicted improved survival using a time-dependent proportional hazards model. The final multivariate model for survival with parameters significant at P </= 0.05 included overall response and pretreatment risk group. Although some of the dosimetric and pharmacokinetic parameters were predictive in univariate analyses, only longer half-**time** of radionuclide in the **blood** showed any indication of improved prediction beyond that provided by the lactic dehydrogenase/Karnofsky performance status-based risk groups. Splenic volume, splenectomy, and malignant tissue Lym-1 reactivity were not contributory. In this patient group, the effect of radiolabeled Lym-1 treatment as indicated by measurable **tumor** response was associated with improved survival. Development of HAMA was also associated with improved survival, indicating that concern about HAMA should not preclude exploration of radioimmunotherapy. Although dosimetry has a role in determining safety based on dose to normal organs, when adjusted for baseline clinical features, dosimetric and pharmacokinetic parameters showed limited ability to improve outcome prediction.

... patients with advanced B-lymphocytic malignancies. Fifty-seven patients were treated with radiolabeled Lym-1 **antibody** in early phase trials between 1985 and 1994. Logistic regression and proportional hazards models were...

...of a partial or complete response (31 of 57 patients) and development of human antimouse **antibody** (HAMA) predicted improved survival using a time-dependent proportional hazards model. The final multivariate model...

...some of the dosimetric and pharmacokinetic parameters were predictive in univariate analyses, only longer half-**time** of radionuclide in the **blood** showed any indication of improved prediction beyond that provided by the lactic dehydrogenase/Karnofsky performance...

... In this patient group, the effect of radiolabeled Lym-1 treatment as indicated by measurable **tumor** response was associated with improved survival. Development of HAMA was also associated with improved survival...

...Tags: Support, U.S. Gov't, Non-P.**H**.S...

...Support, U.S. Gov't, P.**H**.S.

; Adult; Aged; Aged, 80 and over; **Antibodies**, Heterophile--blood --BL; **Antibodies**, Monoclonal; Copper Radioisotopes--pharmacokinetics --PK; Copper Radioisotopes--therapeutic use--TU; Heterocyclic Compounds

--pharmacokinetics--PK; Iodine...
Chemical Name: **Antibodies**, Heterophile; **Antibodies** , Monoclonal; Copper Radioisotopes; Heterocyclic Compounds; Iodine Radioisotopes; Organometallic Compounds; Radiopharmaceuticals; copper-67-2IT-BAT-Lym
?

Biodistribution of filamentous phage-Fab in nude mice.

Yip Y L; Hawkins N J; Smith G; Ward R L
School of Medicine (St. Vincent's Hospital), University of NSW, Sydney, Australia.

Journal of immunological methods (NETHERLANDS) May 27 1999, 225 (1-2) p171-8, ISSN 0022-1759 Journal Code: 1305440
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In vivo panning of peptide libraries in mice has allowed the isolation of peptides which **target** the vasculature of specific organs. The application of this approach to phage displaying Fab fragments (phage-Fab) could lead to the isolation of **antibodies** which recognize novel **tumor** antigens. In this study, we have evaluated the biodistribution of phage-Fab in nude mice. Balb/c nude mice were injected intravenously with 10(9) TU of phage displaying the anti-colon **cancer** Fab c30.6. **Blood** samples were collected at nine **time** points over a period of 72 **h** and three groups of four mice were sacrificed at 4 **min**, 24 **h** and 72 **h**. Normal tissues (liver, colon, spleen, kidneys, lungs, skeletal muscle) and faeces were collected at these time points and the number of viable phage in each sample was determined. The distribution of phage in tissues was also examined by immunohistochemical analysis of paraffin-embedded tissues. Regression analysis of plasma kinetic data showed that the half-life and the volume of distribution of phage was 3.6 **h** and 1 ml, respectively. Phage uptake occurred predominantly in lungs, kidneys, spleen and liver. Relatively few phage were distributed to colon and muscle, and phage were eliminated from the circulation by 72 **h** . Immunohistochemical analysis showed phage to be mainly within the vasculature at 4 **min** , whereas notable phage extravasation was observed at 24 **h** and 72 **h**. In conclusion, this study provides information on the in vivo behavior of phage-Fab which will be useful in the design of in vivo panning strategies. By choosing appropriate time points for tissue collection, it may be possible to isolate novel Fabs against both intra- and extravascular targets.

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? ds

Set     Items   Description
S1    1510505   ANTIBOD?
S2      81382   TIME(5N)(CIRCULATION OR BLOOD)
S3       3788   S1 AND S2
S4    4255232   MIN OR MINUTES OR H OR HOUR
S5        971   S3 AND S4
S6    2924641   TARGET OR CANCER OR TUMOR
S7        185   S5 AND S6
S8     616345   REACH?
S9          5   S7 AND S8
S10         4   RD (unique items)
? s necrosis
     S11  404968  NECROSIS
? s s7 not s11
             185  S7
          404968  S11
     S12     139  S7 NOT S11
? t s12/3,k,ab/1-10

 12/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

16583584   PMID: 15181142
  Radiolabeling, biodistribution, and dosimetry of (123)I-mAb 14C5: a new
mAb for radioimmunodetection of tumor growth and metastasis in vivo.
  Lahorte Christophe M M; Bacher Klaus; Burvenich Ingrid; Coene Elisabeth D
; Cuvelier Claude; De Potter Christian; Thierens Hubert; Van de Wiele
Christophe; Dierckx Rudi A; Slegers Guido
  Department of Radiopharmacy, Faculty of Pharmaceutical Sciences, Gent
University, Gent, Belgium. christophe.lahorte@ugent.be
  Journal of nuclear medicine - official publication, Society of Nuclear
Medicine (United States) Jun 2004, 45 (6) p1065-73, ISSN 0161-5505
Journal Code: 0217410
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  This study reports on the in vitro evaluation, biodistribution, and
dosimetry of (123)I-labeled monoclonal antibody (mAb) 14C5, a new
antibody-based agent proposed for radioimmunodetection of tumor
growth and metastasis in vivo. METHODS: (123)I-mAb 14C5 was prepared by
direct iodination and tested for stability in vitro. Binding assays were
performed on human SK-BR-3 and HeLa carcinoma cells to investigate the
antigen expression, antibody affinity, and kinetics of tracer
binding. For the biodistribution and dosimetry study, 3- to 4-wk-old NMRI
mice were injected intravenously with (123)I-mAb 14C5 (148.0 +/- 7.4 kBq
per mouse) and killed at preset time intervals. Organs, blood,
urine, and feces were counted for radioactivity uptake, and the data were
expressed as the percentage injected dose per gram tissue (%ID/g tissue) or
%ID. The MIRDOSE3.0 program was applied to extrapolate the estimated
absorbed radiation doses for various organs to the human reference adult.
RESULTS: (123)I-mAb 14C5 was obtained in radiochemical yields of 85.0% +/-
2.5% and radiochemical purities were >97%. The iodinated antibody
demonstrated good in vitro stability with 93.6% +/- 0.1% of (123)I-mAb 14C5
remaining intact at 24 h after radiolabeling. (123)I-mAb 14C5 bound
to SK-BR-3 cells (dissociation constant [K(d)] approximately 0.85 +/- 0.17
nmol/L) and HeLa cells (K(d) approximately 1.71 +/- 0.17 nmol/L) with
nanomolar affinity and high specificity, whereas both cell types exhibited
a high CA14C5 antigen expression (maximum number of binding sites [B(max)]
= 40.6 +/- 5.2 and 57.1 +/- 9.6 pmol/L, respectively). In mice, (123)I-mAb
14C5 accumulated primarily in lungs (20.4 %ID/g), liver (15.1 %ID/g), and
```

kidneys (11.1 %ID/g) within 5 **min** after injection. A delayed uptake was observed in stomach (12.8 %ID/g) and urinary bladder (8.7 %ID/g) at 3 and 6 **h**, respectively, after injection. Radioactivity clearance was predominantly urinary, with 44.9 +/- 4.5 %ID excreted during the initial 48 **h** after administration (cumulative amount). The highest absorbed radiation doses determined for the human reference adult were received by the urinary bladder wall (0.1200-0.1210 mGy/MBq), liver (0.0137-0.0274 mGy/MBq), uterus (0.0196-0.0207 mGy/MBq), and lower large intestine wall (0.0139-0.0258 mGy/MBq). The average effective dose resulting from a single (123)I-mAb 14C5 injection was estimated to be 0.017-0.022 mSv/MBq. CONCLUSION: (123)I-mAb 14C5 shows good in vitro biologic activity and favorable biodistribution properties for imaging carcinomas of different origin and provides an acceptable radiation dose to the patient.

Radiolabeling, biodistribution, and dosimetry of (123)I-mAb 14C5: a new mAb for radioimmunodetection of **tumor** growth and metastasis in vivo.
... study reports on the in vitro evaluation, biodistribution, and dosimetry of (123)I-labeled monoclonal **antibody** (mAb) 14C5, a new **antibody**-based agent proposed for radioimmunodetection of **tumor** growth and metastasis in vivo. METHODS: (123)I-mAb 14C5 was prepared by direct iodination...

... performed on human SK-BR-3 and HeLa carcinoma cells to investigate the antigen expression, **antibody** affinity, and kinetics of tracer binding. For the biodistribution and dosimetry study, 3- to 4...
...123)I-mAb 14C5 (148.0 +/- 7.4 kBq per mouse) and killed at preset **time** intervals. Organs, **blood**, urine, and feces were counted for radioactivity uptake, and the data were expressed as the...

... in radiochemical yields of 85.0% +/- 2.5% and radiochemical purities were >97%. The iodinated **antibody** demonstrated good in vitro stability with 93.6% +/- 0.1% of (123)I-mAb 14C5 remaining intact at 24 **h** after radiolabeling. (123)I-mAb 14C5 bound to SK-BR-3 cells (dissociation constant [K...

...ID/g), liver (15.1 %ID/g), and kidneys (11.1 %ID/g) within 5 **min** after injection. A delayed uptake was observed in stomach (12.8 %ID/g) and urinary bladder (8.7 %ID/g) at 3 and 6 **h**, respectively, after injection. Radioactivity clearance was predominantly urinary, with 44.9 +/- 4.5 %ID excreted during the initial 48 **h** after administration (cumulative amount). The highest absorbed radiation doses determined for the human reference adult...
Descriptors: **Antibodies**, Monoclonal--diagnostic use--DU; * **Antibodies**, Monoclonal--pharmacokinetics--PK; *Carcinoma--metabolism --ME; *Carcinoma--radionuclide imaging--RI; *Isotope Labeling--methods--MT ; *Neoplasms...
; Animals; **Antibodies**, Monoclonal--analysis--AN; **Antibodies**, Monoclonal--chemistry--CH; Body Burden; Carcinoma--blood--BL; Carcinoma --urine--UR; Cell Line, **Tumor**--metabolism--ME; Cell Line, **Tumor**--radionuclide imaging--RI; Feces--chemistry--CH; Hela Cells; Metabolic Clearance Rate; Mice; Neoplasms--blood--BL...
Chemical Name: 14C5 monoclonal **antibody**; **Antibodies** , Monoclonal; Radiopharmaceuticals

12/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MED